IN THE UNITED STATES DISTRICT COURT
FOR THE SOUTHERN DISTRICT OF WEST VIRGINIA
AT CHARLESTON

IN RE: ETHICON, INC. PELVIC REPAIR SYSTEMS PRODUCTS LIABILITY LITIGATION	**Master File No. 2:12-MD-02327** **MDL 2327** **JOSEPH R. GOODWIN** **U.S. DISTRICT JUDGE**
THIS DOCUMENT RELATES TO: WAVE 8 CASES ON ATTACHED EXHIBIT A	

REPLY MEMORANDUM IN FURTHER SUPPORT OF PLAINTIFFS' MOTION TO EXCLUDE CERTAIN OPINIONS OF DR. OZ HARMANLI

In further support of their Motion to exclude certain opinions and testimony of Defendants' gynecology expert, Oz Harmanli, M.D. ("Dr. Harmanli"), Plaintiffs state as follows:

ARGUMENT

1. **Dr. Harmanli's opinions on the adequacy of Ethicon's warnings and what other doctors know about the risks of pelvic mesh devices should be precluded pursuant to *Daubert.***

Plaintiffs do not take issue on this motion with Dr. Harmanli's credentials as a physician. Rather, plaintiffs' claim is that Dr. Harmanli opinions are entirely subjective, without reference to any objective source or standard other than stating the IFU is consistent with "the regulations," meaning FDA regulations, which this Court has routinely excluded. *Huskey v. Ethicon*, 848 F.3d 151, 160 (4th Cir. 2017) (evidence regarding compliance with FDA regulations properly excluded by trial court). Moreover, even if this court were to allow evidence regarding the FDA regulations, Dr. Harmanli is not qualified to interpret them, and has not applied a reliable methodology in arriving at his conclusions.

In their brief, Defendants concede that Dr. Harmanli will not offer opinions regarding FDA requirements or regulations or Ethicon's compliance with them, (Defense Brief at 2) but it is clear from Dr. Harmanli's testimony that FDA regulations are the only basis for his warnings opinions in this case. In fact Dr. Harmanli has stated that he does not have an opinion that the warnings in the TVT IFUs are adequate, only that they are consistent with the regulation:

> Q. So, Doctor, I assume that you intend to offer an opinion in this case that the TVT and TVT-O IFUs, or Instructions For Use, are adequate to warn physicians about the risks of the device, right?
>
> A. That is also wrong. **That is consistent with the regulation. That is all I'm saying**[1]

Moreover, Dr. Harmanli's testimony makes is clear that FDA regulations are the only criteria he relies upon for his opinions that the TVT and TVT-O warnings are adequate:

> Q. …I'm just asking in this case, are you relying on anything specifically, other than 21 CFR 801.109(c) for your opinions that the TVT and TVT-O warnings are adequate?
>
> A. Correct
>
> Q. Is there anything else?
>
> A. Yes, the rest of the FDA code. This is just to make it crystal clear that this was cited this way.[2]

This court precluded Dr. Pence's opinions as it related to what should be included in medical device labeling when she was using FDA regulations as a model for the contents of labeling materials. In *Sanchez v. Boston Scientific Corp.*, 2014 WL 4851989 (S.D.W. Va. Sept. 29, 2014), at 35. The same ruling should apply to Dr. Harmanli, who is relying solely on FDA regulations for his opinions regarding adequacy of the TVT IFUs. The opposition brief fails to identify any non-FDA standard or methodology applied by Dr. Harmanli, or standard by which

[1] Dr. Harmanli Dep. Tr., 10-03-2018 Vol. 2. 142:1-6 Plaintiff's Motion, Exhibit D (emphasis added).
[2] Dr. Harmanli Dep. Tr., 10-03-2018 Vol. 1. Plaintiff's Motion, Exhibit C at 65:22-66:5. *See also:* 65:7-21

Dr. Harmanli's opinions on warnings can be objectively evaluated. That gap is fatal to Dr. Harmanli's warning opinions. This Court precluded an expert's warning opinions because the expert applied no standard at all to support his opinions, concluding: "Dr. Slack's subjective and conclusory approach is evidence that his opinion is based on mere speculation and personal belief." *Id.* at *32. Ethicon argues that Dr. Harmanli should be allowed to testify about the sufficiency of product warnings based on his experience in drafting an IFU for a pessary device, similar to the experience Dr. Rosenzweig possesses, which this Court ruled qualified him to offer opinions on the IFU. (Defense Brief at 2). However Dr. Harmanli's opinion here is distinguishable from Dr. Rosenzweig's opinion in *Huskey*. It is not Dr. Harmanli's qualifications as a physician that are it issue, it is his methodology. In this case, as Dr. Harmanli has stated that FDA regulations are the sole basis for his opinions that he TVT IFUs are adequate, and that he is only saying they are "consistent with the regulations," which is his litmus test for adequacy,[3] which was not the case with Dr. Rosenzweig in *Huskey*.

Ethicon's position is that Dr. Harmanli should be permitted to testify concerning the knowledge of the medical community concerning the risks of the pelvic mesh devices. (Defense Brief at 3-4). The fact that Defendants' do not concede that Dr. Harmanli will not offer any opinions regarding the adequacy of the pelvic mesh IFUs, they only concede that he won't offer any legal or regulatory opinions regarding the sufficiency of the IFU is telling, as the obvious inference to be drawn from Dr. Harmanli foundationless opinion that the risks of the pelvic surgery were well known in the medical community, is that they were in fact, adequate.[4] This transparent effort to justify the expert's deficient methodology should not be allowed, as it is essentially asking the court to allow Dr. Harmanli to offer opinions regarding the adequacy of the

[3] *Id*. at 52:25-53:11; 60:8-12; 65:4-6

pelvic mesh IFUs without applying any objective standard and without any foundation for the factual basis of the opinion other than the witness's speculative personal beliefs about what he thinks other doctors already know. Dr. Harmanli has performed no reliable or analysis of what surgeons did or did not know, which is necessary in order to support a valid opinion that a warning was not necessary on any particular issue. Dr. Harmanli admitted he lacked any foundation to opine as to what surgeons generally knew about the risks of pelvic surgery with mesh and had done no formal analysis:

> Q. Have you ever done any kind of survey or formal analysis or study of what risks the pelvic floor surgeons knew about the TVT and TVT-O at any given time?
> A. I have not done a study like that.
>
> Q. So would you agree with me that your opinion that the risks of the TVT and TVT-O are commonly known to surgeons isn't based on any formal analysis?
> A. I would say it's based on the inherent nature of pelvic surgery, that the risks of any pelvic surgery is well known to everyone else. That includes the application of slings in form of TVT or TVT-O

Thus, Dr. Harmanli has done no analysis as to the risks specific to the TVT or TVT-O, he instead relies on his perception of what other surgeons know a about pelvic surgery. He has done no formal analysis of any kind, nor has he studied the question of what risks specific to the TVT and TVT-O are commonly known to surgeons. Dr. Harmanli's opinions are unreliable as he: 1). assumes all the TVT and TVT-O have the same risks as all pelvic surgeries, and 2). assumes that all doctors have the same knowledge he has without any reliable basis or methodology in arriving at these conclusions. For the opinion that the risks were well known to physicians, we simply have Dr. Harmanli's say so, which is insufficient under *Daubert*. *See Kumho Tire Co. v. Carmichael*, 526 U.S. 137, 157 (1999) (stating that "nothing in either *Daubert* or the Federal

Rules of Evidence requires a district court to admit opinion evidence that is connected to existing data only by the *ipse dixit* of the expert").

Allowing the subjective, unsupported opinions by Harmanli regarding the knowledge of the medical community concerning the risks of the pelvic mesh devices should not be permitted under *Daubert.* Moreover, allowing such opinions would create FRE 401 and 403 issues in these cases, as the natural conclusion the jury will draw from this testimony is that the warning provided by defendants' was adequate, despite the expert applying no objective standard to arrive at that conclusion. While Defendants' appear to concede that Dr. Harmanli will not state that the Ethicon's warnings were adequate according to legal or regulatory standards, that is the only standard which he has applied. They appear to make no such concession that Dr. Harmanli will not offer any opinions regarding the adequacy of Defendants' warnings in general, in an attempt to shoehorn FDA evidence and FDA standards into this case. This is despite being unable to point to any objective non-FDA standard applied by Dr. Harmanli. Thus, Dr. Harmanli's warning opinions should be precluded.

II. Dr. Harmanli is not qualified to give opinions on the design of the mesh products, has relied on no objective standard in reaching his conclusions about the risks and benefits of the mesh products, and his opinions should be excluded.

Dr. Harmanli is admittedly not an expert in design, and Defendants appear to concede that he is not offering any opinions on design, but rather is "offering opinions regarding the risks and benefits of the TVT and TVT-O as designed," which is really just clever wordsmithing by Ethicon. (Defense Brief at 5). By offering opinions about the risks and benefits of the TVT, Dr. Harmanli is, in effect, stating that the design is safe and effective and the benefits outweigh the risks. Dr. Harmanli use of mesh products, and his qualifications as a pelvic floor surgeon do not, by themselves, uniquely qualify him to opine regarding the safety and efficacy of a medical

device any more than a licensed driver is qualified to opine about the safety of a vehicle based on how it feels when he drives it and based on what he has observed when others drive it. Defendants claim that the foundation of Dr. Harmanli's design opinions (which they characterize as risks, benefits, and alternatives opinions) is his "extensive clinical experience and literature review." (Defense Brief at 7). A review of the literature does not provide sufficient basis for Dr. Harmanli to offer a reliable design opinion unless he can identify an appropriate standard that she applied. *See Winebarger v. Boston Scientific Corp.*, No. 2:13-CV-28892, 2015 WL 1887222, at *14 (S.D. W. Va. Apr. 24, 2015) (finding that Dr. Schull had not reliably applied the principles learned through his experience and the literature to the facts of this case because he had not seen any standard operating procedures or design protocols for the development of the medical device in question).

Here, in addition to admitting not being an expert in design, Dr. Harmanli has applied no objective standard for his opinions that the TVT devices are safe and effective:

> Q. So how high would the erosion rate need to be for an SUI device before you started looking looking into it as a serious concern?
>
> A. **I don't have a magic number.** I want to look at it from again from efficacy, safety, and everything else, ease of use, utility, desirability cost, all of that would have to play a role in my decision making
>
> Q. Can we agree that it's got to be somewhere between 2 and 30 percent, because the TVT, you think has a 2 percent erosion rate, and 30 percent makes you uncomfortable, so somewhere in that range?
>
> A. Correct, that makes sense.
>
> Q. But as you sit here to today you can't put a number on it, right?
>
> A. I don't want to set a bar there[5]

[5] Plaintiff's Motion, Exhibit C at 102:23-103:12

More troubling is that Dr. Harmanli's analysis of the risks and benefits of the TVT and TVT-O device is unreliable as he consistently ignores evidence which does not support his opinion that the erosion rate and/or complication rate with the TVT products is "low," including information which once appeared on Ethicon's own website that the erosion rate for TVT was 19%[6]:

> Q. And you've never told – in fact, it sounds like you were not aware that at one point Ethicon reported that 19 percent erosion rate on their website
> A. I was not aware.
> Q. So obviously, if you weren't even aware of it, that's not something you would have ever reported to a patient; right?
> A. I was not aware of that. And it's not valuable information for the clinician and scientist, it's an outlier. [7]

Dr. Harmanli disregards information supplied by Ethicon's own website when forming opinions regarding the risks and benefits of the TVT when it does not support his conclusion and simply labels it an "outlier". Dr. Harmanli also admits he ignores product complaints and case reports published in the peer-reviewed medical literature.[8] Nowhere does Dr. Harmanli or Ethicon identify any objective standard applied by Dr. Harmanli or by which Dr. Harmanli's opinions on safety and efficacy can be tested or objectively evaluated and his methodology is not reliable as he consistently fails to consider evidence which does not support his opinions that the benefits of the TVT outweigh the risks. As such, he should be precluded from giving any opinions related to the adequacy of the design, safety, and efficacy of the mesh products.

III. Dr. Harmanli's opinion there is no clinical difference between mechanically cut versus laser cut mesh with respect to the effectiveness or safety in the medical literature is not reliable.

[6] Ex. A to Plaintiff's reply, Ethicon Website capture taken on 9-18-2013
[7] Plaintiff's Motion, Exhibit C at 106:21-107:6
[8] Plaintiff's Motion, Exhibit C at 157:3-158:20

Plaintiffs have argued that there is no reliability to Dr. Harmanli's methodology in concluding that there is no clinical difference between mechanically cut versus laser cut mesh with respect to safety and effectiveness on two grounds: 1). that the only two pieces of medical literature that support his position were essentially put in his report only because Ethicon's counsel told him that they supported the opinion, and 2). Dr. Harmanli relies on his personal experience with mechanically cut versus laser cut mesh in arriving at this opinion, yet he admits he can't tell the difference between laser cut and mechanically cut mesh. This is essentially a litigation-driven opinion supported only by counsel for Ethicon.

Dr. Harmanli admitted that the only two pieces of medical literature he relied on for this opinion was the Rusavy study and the Thubert paper.[9] He further admitted that he relied on the Thubert paper without knowing how many devices in that study were mechanically cut versus laser cut because attorneys for Ethicon told him it supported his position,[10] and admitted that in the Rusavy study there the question of clinical outcomes was "not studied very well" and that there were many other things "they were not doing right" in that study.[11] Relying on a study simply because lawyers told Dr. Harmanli that it supported his opinion without looking into the specifics of the study should be considered a reliable methodology under *Daubert*.

Further, Dr. Harmanli relies on his clinical experience for this opinion, yet his own testimony indicates he cannot tell the difference between laser cut and mechanically cut mesh, therefore, his conclusion that there is no difference is fundamentally flawed as we have no way of knowing if Dr. Harmanli has even used laser cut mesh in his practice, let alone how many times he has used it compared to laser cut mesh:

[9] Plaintiff's Motion, Exhibit D at 160:25-161:19
[10] *Id.* at 162:25-163:9
[11] *Id.* at 164:12-165:11

Q. Do you know – if you pick a TVT retropubic off the shelf, do you know how to even tell whether or not it's a mechanically cut or a laser cut?
A. I do not.[12]
***
Q. But I think as we covered earlier, you don't even know how to tell the difference if a device is sitting on the shelf whether or not it is mechanically or laser cut mesh, right?
A. Correct. I have no way of knowing that. [13]

Dr. Harmanli admits that his opinion on the clinical difference in his practice is not based on any formal or scientifically rigorous analysis.[14] Nothing in Ethicon's response addresses these two fatal flaws in Dr. Harmanli's methodology in arriving at his conclusions on this issue.

IV. Dr. Harmanli should be precluded from offering precise statistics regarding his own personal experiences with the mesh, including that there is no difference between laser cut mesh and mechanically cut mesh

Ethicon cites *Bellew v. Ethicon*,[15] for the proposition that this court should allow Dr. Harmanli to offer opinions and testimony regarding his general personal experiences with mesh products. Def. Mem. at 8-10. However, the situation with Dr. Harmanli is wholly distinguishable from *Bellew*. Here, Dr. Harmanli wishes to offer an opinion there is no clinical difference between the laser cut and mechanically cut TVT meshes in his practice, but this opinion suffers from the fatal flaws in methodology and reliability as outlined in section III. above, and in sections III. and IV. of plaintiffs' memorandum, which were not present in the methodology used by Dr. Robboy in the *Bellew* case. Moreover, it appears that Ethicon would like Dr. Harmanli to testify that he has "minimal complications in his clinical practice," which was on par with the studies he cites through his expert report. (Defense. Brief at 9). Essentially,

[12] Plaintiff's Motion, Exhibit C at 21:15-18
[13] Plaintiff's Motion, Exhibit D at 160:14-18
[14] *Id*. at 160:19-24
[15] Def. Mem. at 9

this amounts to testifying to a 2% erosion rate,[16] with no foundation or reliable methodology in arriving at these precise statistics, which is exactly the kind of testimony this court has excluded in the past. *See In re Ethicon*, 2016 WL 4542054 (S.D. W. Va. 2016). Moreover, Dr. Harmanli's methodology in arriving at this conclusion suffers from the fatal flaws of ignoring, among under things: 1). data from Ethicon's own website indicating a 19% erosion rate, 2). product complaints to the company, and 3).case reports in the peer-reviewed published medical literature as outlined in section III. above. Therefore, this court should exclude Dr. Harmanli from testifying as to his personal experiences with the mesh products in this case.

V. Dr. Harmanli should be precluded from testifying that polypropylene does not degrade.

Nothing in the Defendants' response addresses the fatal flaws in Dr. Harmanli's qualifications and methodology in arriving at his conclusion that polypropylene does not degrade. (Defense Brief at 10-12). Dr. Harmanli testified that he was not aware that the manufacturer of the raw polypropylene which goes into the TVT and TVT-O has warned that strong oxidizers, such as peroxides, are incompatible with the TVT and TVT-O.[17] Dr. Harmanli admits that he is aware that the vaginal region is a natural source of peroxides, but he has not studied the question of whether or not the peroxides in the vagina affect the composition of the TVT mesh.[18] Dr. Harmanli simply has not reviewed the necessary and relevant documents regarding degradation—including the MSDS for the products, and the testimony of Ethicon's designated witness on the topic of polypropylene degradation—and instead, he just insists that polypropylene mesh does not degrade. Dr. Harmanli's opinion that degradation does not occur,

[16] Plaintiff's Motion, Exhibit C at 27:16-18
[17] Ex. D to Plaintiffs' Motion at 184:12-19. *see also* Ex. F to Plaintiff's Motion, Material Safety Data Sheet for Polypropylene used in the TVT products at page 4: "The following materials are incompatible with this product: Strong oxidizers such as ….peroxides…"
[18] Ex. D to Plaintiff's Motion at 184:21-185

or that it is not "clinically relevant," should be excluded because it is neither supported by his review and understanding of the scientific material, nor by scientifically reliable clinical experience.

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Respectfully submitted,

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CERTIFICATE OF SERVICE

I hereby certify that on November 1, 2018, I electronically filed the foregoing document with the Clerk of the Court using the CM/ECF system which will send notification of such filing to the CM/ECF participants registered to receive service in this MDL.

s/ Jeffrey M. Kuntz